Original Article

DOI: 10.7860/JCDR/2018/35838.11514

Internal Medicine Section

Trends in Septicaemic Patients Admitted in Tertiary Care Teaching Hospital in Andhra Pradesh, India

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ABSTRACT

Introduction: Septicaemia is one of the significant causes of morbidity and mortality in Intensive Care Units (ICUs). The rate of antimicrobial resistance in ICU is very high compared to general hospital setting.

Aim: To enumerate common bacterial pathogens causing sepsis and to identify their antimicrobial susceptibility pattern.

Materials and Methods: This was a retrospective descriptive study done in patients with sepsis during January 2016 to December 2017. The Institutional Ethical Committee clearance was obtained. Data were collected from inpatient case files regarding clinical history, laboratory parameters with special reference to causative organisms and antibiotic sensitivity pattern. Data were entered in Microsoft Excel sheet and analysed using strata 14.0.

Results: Among 216 subjects of sepsis admitted to ICU during study period, 130 (60.1%) were males, with mean age of 52.83 year (±16.6 SD). Pneumonia (31.94%) was the major cause of sepsis followed by urosepsis. Gram negative organisms were the major cause of sepsis accounting for 76.25% of organisms isolated. *Escherichia coli* was the most common organism isolated in urine (65.9%) and blood cultures (32%). All Gram negative bacteria had high level of resistance to Amoxicillin Clavulunic Acid (Amoxyclav) (85.9%), ampicillin sulbactum (66.7%) and third generation cephalosporins (70%).

Conclusion: Gram negative organisms were the principal causes of septicaemia. Cephalosporin resistance was more than 70%. *Acinetobacter* species was resistant to most antibiotics. The knowledge of bacterial profile of sepsis and antibiotic susceptibility pattern not only helps in improving outcome but also prevents emergence of drug resistance strains.

Keywords: Antimicrobial sensitivity, Cephalosporin resistance, Gram negative organisms, Septicaemia

INTRODUCTION

Septicaemia is one of the major causes of morbidity and mortality in patients admitted to ICUs worldwide [1]. The systemic, deleterious host response to infection is defined as sepsis [2]. Systemic Inflammatory Response Syndrome (SIRS) is the presence of two or more of the following conditions: abnormal body temperature (<36°C (96.8°F) or >38°C (100.4°F); heart rate (>90 beats/minute); respiratory rate (>20 breaths/minute); and White Blood Cell (WBC) count (<4000/mm^3 or >12,000/mm^3). SIRS of infectious aetiology is called sepsis [2].

The source of infection in sepsis can originate from different regions of the body, usually from lung, urinary tract, abdomen, intravenous catheters, endotracheal tube and so on. Infants and elderly are the most vulnerable for sepsis and so are patients with chronic illnesses like diabetes mellitus, chronic kidney disease, and chronic liver disease [3].

The aetiological agents of sepsis differ widely. Gram negative bacteria with lipopolysaccharide structure are the leading causes of sepsis [3]. In the recent years septicaemia due to Gram positive organisms are on the rise and accounts to nearly half of the incidents of septicaemia [3,4]. Gram positive bacteria do not have endotoxin, but they cause sepsis by releasing exotoxins that act as super antigens (e.g., *Staphylococci aureus* or *Streptococci* spp.) [3].

The bacteria increasingly isolated in sepsis patients include Gram positive organisms like: *Streptococcus pneumonia (S. pneumonia)*, *Streptococcus pyogenes (S. pyogenes), Streptococcus agalactiae (S. agalactiae)*, and *Staphylococcus aureus (S. aureus)*. Among Gram negative bacteria *Neisseria meningitides, Escherichia coli (E. coli), Klebsiella pneumoniae (K. pneumoniae), Proteus, Enterobacter, Serratia, Citrobacter, Pseudomonas aeruginosa (P. aeruginosa)* and *Acinetobacter* are frequently isolated [3].

The comprehensive management protocol for sepsis and septic shock includes early diagnosis and initiation of empirical antibiotics along with supportive therapy [5]. The appropriate use of an empirical antibiotic is essential to reduce the mortality rate of sepsis [6] and should be started within 1-2 hours of diagnosing of severe sepsis. Emergence of multi drug resistant bacteria has posed a serious problem by compromising effective empirical antimicrobial therapy and increasing economic burden [7]. The irrational use of antibiotics, usage of sub therapeutic doses and unregulated over the counter sale of antibiotics are the possible reasons for spread of multi drug resistant pathogens in the community [8].

As there is a change in aetiological agents causing septicaemia in the recent years [4], current study was undertaken to enumerate the common bacterial pathogens in sepsis. We also aimed to identify the antimicrobial susceptibility pattern in patients with sepsis so as to help in formulating suitable empirical antimicrobial therapy for septicaemia.

MATERIALS AND METHODS

This was a retrospective descriptive study conducted in Medical ICU of PES Institute of Medical Sciences and Research (PESIMSR) Hospital in Andhra Pradesh, India, during January 2016 to December 2017. Patients over the age of 18 years admitted to Medical ICU with the diagnosis of sepsis were included in the study. Patients less than 18 years were excluded from this study. As it is a retrospective study, informed consent was not obtained. Institutional Ethical Committee clearance was obtained. Patients were categorised as sepsis, severe sepsis, septic shock and Multi Organ Dysfunction Syndrome (MODS) as per standard definitions [9].

Systemic Inflammatory Response Syndrome (SIRS): Two or more of the following conditions: (1) fever (oral temperature >38°C) or hypothermia (<36°C); (2) tachypnoea (>24 breaths/minute);

(3) tachycardia (heart rate >90 beats/minute); (4) leukocytosis (>12,000/L), leucopenia (<4,000/L), or >10% bands; may have a non infectious aetiology.

Sepsis: SIRS that has a proven or suspected microbial aetiology.

Severe sepsis: Sepsis with one or more signs of organ dysfunction.

Septic shock: Sepsis with hypotension (arterial blood pressure <90 mmHg systolic, or 40 mmHg less than patient's normal blood pressure) for at least 1 hour despite adequate fluid resuscitation or need for vasopressors to maintain systolic blood pressure more than or equal to 90 mmHg.

Multi organ dysfunction syndrome: Dysfunction of more than one organ, requiring intervention to maintain homeostasis [9].

Data were collected from inpatient case files of patients admitted to ICU. The information obtained includes baseline demographic data, clinical history and laboratory data. Clinical variables studied were age, gender, duration of hospital stay, place of stay, income/profession. Details were collected about the source of infection, previous comorbidities, and empirical treatment was given. The causative agents and the sensitivity pattern of the organisms were collected from case records.

STATISTICAL ANALYSIS

All the details were entered in Microsoft excel sheet. Data analysis was done using Strata 14.0. The descriptive data were analysed as follows: categorical data were analysed using percentages and the continuous data were analysed using mean and standard deviation. For inferential statistics, diagnostic test and chi-square test was used. A probability value of less than 0.05 was considered as statistically significant.

RESULTS

There were 1240 patients admitted to ICU from January 2016 to December 2017, of which 216 patients with diagnosis of sepsis who fulfilled the inclusion criteria were included in the study. Among 216 patients, 130 (60.19%) were males, 86 (39.81%) females. The mean age of patients was 52.83 years (±16.6 SD). Majority (n=141, 65.28%) of the patients were from rural areas. In terms of primary source of infection, pneumonia (n=69, 31.94%) and urinary tract infection (n=48, 22.22%) were the common causes of sepsis in this study. The clinical characteristics of the patients is depicted in [Table/Fig-1]. The mean quick Sequential Organ Failure Assessment (qSOFA) score was 1.29 (±1.12 SD). C-reactive Protein (CRP) was positive in 131 (60.65%) patients and serum lactate levels high in 112 (51.8%) patients.

The empirical antibiotics commonly used were Amoxyclav (n=57, 26.38%), piperacillin tazobactum (n=68, 31.4%) and third generation cephalosporins (n=71, 32.8%). Combinations of amoxicillin clavulunic, amikacin (n=8, 3.7%) and amoxicillin clavulunic, metronidazole (n=12, 5.5%) were used in rest of patients.

In present study, out of 216 culture samples analysed, at least one organism was isolated in 139 (64.35%) patients either from samples of blood, urine, sputum, pus, endotracheal aspirate. Among the samples which tested positive for growth of microbes, pus had the highest yield (n=33,100%), followed by endotracheal aspirate (n=24, 57.14%) and urine cultures (n=47, 44.76%). In the present study of 216 blood cultures, only 25 were culture positive yielding culture positivity rate of 11.5%.

The frequency of isolation of Gram negative bacteria (n=106, 76.25 %) was higher than that of gram positive bacteria (n=33, 23.7%). *Escherichia coli (E. coli)* (n=40, 28.7%), was the most common organism isolated from cultures, followed by *Klebsiella pneumonia (K. pneumonia)* (n=28, 20.1%), *Pseudomonas aeruginosa* (*P. aeruginosa*) (n=16, 11.51%) and *Staphylococcus aureus (S.aureus)* (n=9, 6.4%). The organisms isolated in the present study are shown in [Table/Fig-2].

Character	Mean	SD	Min	Max
Age (years)	52.83	16.66	18	86
Hospital stay (in days)	8.314	8.56	0.5	86
	Frequency		Percent	
Gender				
Male	130		60.19	
Female	86		39.81	
Locality				
Urban	75		34.72	
Rural	141		65.28	
Socioeconomic status				
APL	74		34.26	
BPL	142		65.74	
Primary source of infection				
Respiratory (Pneumonia)	69		31.94	
Urinary tract infection (UTI)	48		22.22	
Intra abdominal	17		7.87	
Central Nervous System (CNS)	9		4.17	
Skin and soft tissue	31		14.35	
Lung and Genito urinary	21		9.72	
CRBSI	2		0.93	
Others *	19		8.79	
Previous comorbidities				
Diabetes mellitus	73		33.80	
Hypertension	59		27.31	
Chronic Kidney Disease	25		11.57	
Tuberculosis	14		06.48	
COPD	37		17.13	
Cirrhosis	18		08.33	
IHD	28		12.96	

[Table/Fig-1]: Clinical characteristics of patients admitted to ICU (n=216).
SD: Standard deviation; Min: Minimum; Max: Maximum
APL: Above poverty line; BPL: Below poverty line; CRBSI: Catheter related blood stream infection; COPD: Chronic obstructive lung disease; IHD: Ischaemic heart disease.
*Respiratory+soft tissue = 4, UTI+Intra abdominal = 6, respiratory+CNS =3, respiratory+Intra abdominal=6

Organism	Frequency	percentage
Escherichia coli	40	28.7
Klebsiella pneumonia	28	20.1
Pseudomonas aeruginosa	16	11.5
Enterococcus	8	5.7
Acinetobacter species	11	7.9
Staphylococcus aureus	9	6.4
Streptococcus spp.	7	5.0
Methicillin resistant *Staphylococcus aureus*	5	3.5
Methicillin resistant Coagulase negative *Staphylococcus aureus*	4	2.8
Coagulase negative *Staphylococcus aureus*	2	1.4
Citrobacter	2	1.4
Enterobacter	1	0.7
Total cultures positive	139	64.35
No growth	77	35.65

[Table/Fig-2]: Frequency of Organisms isolated from patients admitted with sepsis n=216, n (%).

Among patients with pneumonia, *K. pneumonia* (n=19, 40.4%) was the predominant organism isolated followed by *P. aeruginosa* (n=13, 27.6%). The organisms isolated from various samples collected are shown in [Table/Fig-3].

Antibiotic resistance pattern of Gram negative bacteria isolated [Table/Fig-4] revealed a high rate of resistance amongst all bacteria

Organism	Blood	Urine	Pus	Sputum	ET
E.coli	8 (32)	31 (65.9)	4 (12.1)	-	-
K. pneumonia	5 (20)	2 (4.2)	4 (12.1)	10 (43.4)	9 (37.5)
Proteus mirabilis	0	1 (2.1)	2 (6.0)	0	0
Proteus vulgaris	0	2 (4.2)	1 (3.0)	0	0
S. aureus	0	1 (2.1)	5 (15.1)	1 (4.3)	0
P. aeruginosa	1 (4)	0	4 (12.1)	7 (30.4)	6 (25)
Streptococcus	0	0	3 (9.0)	4 (17.3)	1 (4.1)
Enterococcus	1 (4)	3 (6.3)	2 (6.0)	0	1 (4.1)
Enterobacter	0	1 (2.1)	0	0	0
CONS	1 (4)	1 (2.1)	0	0	0
Acinetobacter spp.	6 (24)	2 (4.2)	2 (6.0)	1(4.3)	5 (20.8)
MRSA	1 (4)	1 (2.1)	5 (15.1)	0	0
Citrobacter	1 (4)	1 (2.1)	0	0	1 (4.1)
MRCONS	1 (4)	2 (4.2)	1 (3.0)	0	1 (4.1)
Total cultures positive	25	47	33	23	24
No growth	191	58	0	29	18
Culture positivity rate	11.5%	44.76%	100%	44.23%	57.14%

[Table/Fig-3]: Frequency of organisms isolated based on source, n (%).
CONS: Coagulase negative *Staphylococcus aureus*, MRCONS: Methicillin resistant negative *Staphylococcus aureus*, MRSA: Methicillin resistant *Staphylococcus aureus*

Organism	*E. coli* (n=40)		*K. pneumonia* (n=28)		*P. aeruginosa* (n=16)		*Proteus mirabilis* (n=3)		*Proteus vulgaris* (n=3)		*Acinetobacter* spp. (n=11)	
Antibiotic	S	R	S	R	S	R	S	R	S	R	S	R
Amikacin	77.5	7.50	50	39.2	75	12.50	33.33	66.67	100	0	36.36	63.64
Amoxyclav	15	85	10.7	89.29	12.5	87.5	66.67	33.33	33.3	66.67	9.09	90.9
Ampicillin Sulbactum	20	75	7.14	75	6.25	87.5	33.3	66.7	66.7	33.3	0	100
Cefepime	27.5	60	25	67.86	52.5	37.5	33.3	66.6	33.3	66.6	27.27	72.3
Cefixime	10	90	7.14	82.14	12.5	81.25	66.7	33.3	0	100	10.1	90.9
Cefotaxime	10	87.5	17.86	75	12.5	87.5	33.3	66.7	0	100	10.1	90.9
Cefpodoxime	7.5	90	14.29	78.57	18.75	68.75	33.3	66.7	33.3	66.7	0	100
Ceftazidime Clavulunic acid	15	77.5	32.14	53.57	50	50	33.3	66.67	0	100	0	100
Ciplox	12.5	82.5	42.86	42.86	56.25	31.25	66.6	33.3	33.3	66.7	27.27	72.73
Cotrimoxazole	12.5	75	14.29	53.57	6.25	68.75	33.3	33.3	0	100	18.18	72.73
Gentamycin	30	52.50	50	50	75	25	33.3	66.6	66.6	33.33	27.27	72.73
Imipenem	92.5	2.5	78.57	7.14	100	0	100	0	100	0	36.36	45.45
Meropenem	87.5	5.0	78.57	14.29	100	0	100	0	100	0	45.45	36.36
Piperacillin tazobactum	40.6	52.5	39.29	57.14	75	12.5	66.67	33.33	66.67	33.3	27.27	63.64
Ticarcillin Clavulunic acid	17.5	77.5	28.57	64.29	50	37.5	66.67	33.33	33.3	66.67	18.18	63.64

[Table/Fig-4]: Antibiotic resistance pattern of gram negative microorganisms isolated (in %).
S= Sensitivity, R= Resistant

isolated for (Amoxyclav) (33.3-90.9%) and ampicillin sulbactum (66.7-100%). The rate of resistance of Acinetobacter species was found to be more than 90% for drugs like amoxicillin group, cefixime, cefotaxime, cefpodoxime, ceftazidime clavulunic acid. The drugs to which *E. coli* showed high rate of resistance were cefixime (n=36, 90%), cefotaxime (n=35, 87.5%), cefpodoxime (n=36, 90%), ceftazidime clavulunic acid (n=31, 77.5%), piperacillin tazobactum (n=21, 52.5%), and ticarcillin clavulunic acid (n=31, 77.5%). The rates of resistance of Gram negative bacteria were least to imipenem and meropenem except for Acinetobacter species which exhibited (n=5, 45.45%) and (n=4, 36.3%) resistance to these drugs respectively.

The antibiotic resistance pattern of Gram positive bacteria isolated is depicted in [Table/Fig-5]. The rates of resistance of *S.aureus* to various antimicrobials used are amoxyclav (n=6, 66.6%), ampicillin sulbactum (n=9,100%), cefepime (n=3, 33.3%), amikacin (n=1, 11.1%), gentamycin (n=1, 11.1%), piperacillin tazobactum (n=5, 66.6%). All isolates of *S.aureus* were 100% sensitive to vancomycin (n=9) and rifampicin (n=9). Streptococcus species remained sensitive to amoxyclav (n=7, 100%), ampicillin sulbactum (n=5, 71.4%), amikacin (n=6, 85.7%) and gentamycin (n=6, 85.71%).

In present study patients were categorised as sepsis (n=98, 45.3%), severe sepsis (n=23, 10.6%) septic shock (n=60, 27.7%) and MODS (n=35, 16.2%). The mortality rate (in hospital) was 25% (n=54), out of which 60% (n=21) of patients with MODS and 41.6% (n=25) of patients with severe sepsis died.

During the hospital stay, 62.9% (n=136) of patients developed one of the complications. Acute renal failure (n=46, 33.8%) was the predominant complication followed by acute respiratory distress syndrome (n=25, 18.38%) as shown in [Table/Fig-6].

DISCUSSION

Sepsis is the one of the leading causes of mortality in patients admitted to ICU [10]. The delay in administration of antibiotics increases the morality rate by 7% [11]. The rate of antimicrobial resistance in ICUs is very high compared to general hospital setting [12]. In this present study, antimicrobial resistance pattern of 139 bacterial strains isolated has been studied. The mean age of patients was 52 years and septicaemia was more common among males (60%). Culture positivity rate was 64.35%, blood culture being positive in 11.5%. A study done in Delhi by Alam MS et al., showed culture positivity rate of 20.9% and septicaemia in 65.6% of males [13]. However, a study in Vietnam had equal incidence of septicaemia in males and females [14]. In a

Organism	*S. aureus* (n=9)		MRSA (n=5)		*Streptococcus* (n=7)		CONS (n=2)		MRCONS (n=4)		Enterococci (n=8)	
Antibiotic	S	R	S	R	S	R	S	R	S	R	S	R
Amikacin	88.89	11.11	80.00	20.00	85.71	14.29	50.00	50.00	50.00	0	12.5	75.00
Amoxyclav	33.33	66.67	0	100	100	0	50	50	0	100	50	37.5
Ampicillin Sulbactum	0	100	20	80	71.43	0	50	50	0	100	62.5	37.5
Cefepime	11.1	33.3	0	100	14.29	28.57	0	100	0	75	0	75
Cefixime	0	33.3	0	80	14.2	28.5	50	50	0	75	0	75
Cefotaxime	0	33.3	0	80	14.29	28.57	50	50	0	75	0	75
Ofloxacin	33.3	0	40	0	71.43	14.29	50	0	25	0	25	12.5
Cotrimoxazole	33.33	22.22	60	20	28.57	57.14	0	100	0	100	0	100
Gentamycin	55.56	11.11	60	40	85.71	14.29	0	0	0	100	12.5	87.5
Piperacillin tazobactum	44.44	66.66	0	80	28.57	0	0	50	50	50	50	25
Clindamycin	77.78	22.22	40	60	71.43	14.29	0	100	50	50	0	75
Vancomycin	100	0	80	20	85.71	14.29	100	0	100	0	87.5	12.5
Teicoplanin	88.89	11.11	100	0	71.43	28.4	100	0	50	50	100	0
Rifampicin	100	0	100	0	85.71	14.29	0	0	50	50	25	37.5

[Table/Fig-5]: Antibiotic resistance pattern of gram positive microorganisms isolated (in %).
CONS: Coagulase negative *Staphylococcus aureus*, MRCONS: Methicillin resistant negative *Staphylococcus aureus*, MRSA: Methicillin resistant *Staphylococcus aureus*
S: Sensitivity, R: Resistant

Complications	Number (%)
Nil	80 (37.03%)
Acute kidney injury	46 (33.82%)
Acute respiratory distress syndrome	25 (18.38%)
Hepatitis	10 (7.35%)
INR derangement	20 (14.70%)
Multiple	35 (25.73%)

[Table/Fig-6]: Frequency of complications in sepsis patients (n=216).

study by Orsini J et al., median age of patients was 64 years and culture positivity rate was 12.6% [7]. Studies done in India and other countries also had similar findings [15-17]. Angus DC et al., stated that incidence of severe sepsis increases more than 100 fold with age [18]. It is also debatable whether decreased incidence of sepsis in females is due to increased oestrogen hormone, influencing greater activity of immune system and increased cytokine activity in females [19].

In this study Gram negative bacteria (76.2%) were the predominant organisms isolated from sepsis patients. *E. coli* was the most common organism isolated followed by *K. pneumonia, P. aeruginosa*, *Acinetobacter* spp. An epidemiological study done by Chatterjee S et al., in eastern India over 5 years had Gram negative bacteria isolated in 73.4% of patients [20]. The common Gram negative organisms isolated were *Acinetobacter, P. aeruginosa, K. pneumonia* and *E. coli* [20]. In a study done in northern India, 80.96% of isolates causing blood stream infections were by Gram negative organisms, majority of them by *P. aeruginosa* (19.75%), *E. coli* (15.17%) and *K. pneumonia* (14.99%) [21]. Predominant Gram negative bacterial sepsis was also found in other studies across India [13,22,23]. In a study done in China Gram negative organisms were isolated in 62% and Gram positive organisms in 44% of patients with sepsis [24]. However, a study done by Martin GS et al., in the United States found predominance of Gram positive bacteria being isolated in sepsis in the recent years [25]. Several studies have shown predominant isolation of Gram positive bacteria in sepsis in the recent years [15,26-28]. The microorganisms causing sepsis have changed over many years [25]. The difference in distribution of pathogens could be explained based on epidemiological differences of aetiological agents, population studied and geographic locations.

The sources of sepsis are commonly from respiratory infections, genitourinary and abdominal infections and respiratory infections are responsible for nearly half of all patients of sepsis [25,26]. In the present study, respiratory infections were the most common cause of sepsis (31.94%) followed by urosepsis.

The risk of infection in ICU is very high due to vulnerable population, use of invasive devices and multiple drugs [12]. Along with infection the burden of antimicrobial resistance significantly increases clinical and economic burden [12]. One of the reasons for increasing rate of antimicrobial resistance is use of broad spectrum antibiotics [29]. The factors responsible for further emergence and spread of multidrug resistant pathogens are induction, selection, introduction and dissemination of resistant strains [29]. A salient finding from this study was the extent of antimicrobial resistance found among both Gram negative and Gram positive organisms. A very high degree of resistance was noted among all Gram negative organisms including *E. coli* to cephalosporins (90%) and amoxicillin group of drugs (85-90%). This can be attributed due to wide spread use of cephalosporins and spread of CTX-M type of Extended Spectrum β-Lactamases (ESBLs) [30]. Among *E. coli* isolates the degree of resistance was least to amikacin (7.5%), imipenem (2.5%) and meropenem (5.0%). In a recent study done in China [31], the rate of resistance of *E. coli* to various drugs were: ampicillin (91.6%), Sulfamethoxazole and Trimethoprim (SMZ-TMP) (80.6%), ampicillin/sulbactam (79.5%), ciprofloxacin (74.1%), and levofloxacin (73.5%). In the same study carbapenems had highest in vitro activity against *E. coli* strains (94.0%), followed by amikacin (92.0%) and piperacillin/tazobactum (80.6%) [31]. Studies done by Alam MS et al., and Renuga S et al., had comparable findings [13,15]. In an effort to prevent carbapenem resistance, amikacin can be considered in empirical treatment of *E. coli* in settings with high prevalence of ESBL producing *E. coli* [30].

Klebsiella pneumonia was the primary aetiological agent isolated from respiratory infections in the current study (39.5%). *Among K. pneumonia* isolates, least resistance was identified for imipenem (7.14%) and meropenem (14.29%). The degree of resistance to amikacin was 39.2% and gentamycin 50%. The study done by Kumar AR, found *K. pneumonia* to be a key pathogen isolated in pneumonia (39.5%) and *K. pneumonia* being least resistant to amikacin (7.3%) [32]. Similar findings were observed in separate studies [14,24]. Due to the production of ESBLs, which are plasmid mediated, the resistance in *K. pneumonia* is difficult to treat and control, leading to outbreaks [12].

Acinetobacter species has shown striking resistance to many antibiotic classes in previous studies [13,24]. In a study done in Vietnam, *Acinetobacter* species had more than 90% resistance to *cephalosporins,* fluroquinolones, carbapenems, including 1.5% resistance to colistin [14]. In our study *Acinetobacter* species had 100% resistance to most *cephalosporins* and ampicillin sulbactum.

The degree of resistance to carbapenems was more than 35%. All isolates tested remained 100% sensitive to colistin. Emergence of multidrug resistant *Acinetobacter* in hospital acquired infections is a great challenge for physicians as it reduces the treatment options and significantly increases the healthcare costs.

Infections by *P. aeruginosa* cause significant increase in healthcare costs and mortality. It is the most common cause of bacterial sepsis associated with nosocomial infections in ICU [33]. In the present study, *P. aeruginosa* was second most common organism isolated in respiratory infections. All isolates tested 100% sensitive to imipenem and meropenem. The rate of resistance to amikacin (12.5%) and piperacillin tazobactum (12.5%) were least among other tested antimicrobials. Arora D et al., identified the following resistance pattern among *P. aeruginosa*: imipenem (3.7%), amikacin (41.5%), ciplox (73.2%), piperacillin-tazobactum (44%) [34]. Appropriate initial antimicrobial administration for *P. aeruginosa* infections showed significant improvement in hospital survival [35].

Gram positive *bacteremia* accounted for 23.7% cases of septicaemia in our study. *S. aureus* (27.2%) was the predominant gram positive organism isolated followed by *Enterococcus* (24.2%), *Streptococcus* (21.2%) and Methicillin Resistant *Staphylococcus aureus* (MRSA) (15.1%). In previous studies conducted in India by Renuga S et al., organisms isolated were *S. aureus* (30.61%) and Coagulase Negative *Staphylococcus aureus* (25.8%) [15]. Ethiopian studies done by Dagnew M and Kumalo A also have *S. aureus* isolated in 23.9% and 40% of patients respectively [17,28]. *S. aureus* and MRSA were the most common organisms isolated from pus in this study. *S. aureus* had 100% resistance to ampicillin sulbactum. MRSA showed high rates of resistance to ampicillin (80%), cefepime (100%), piperacillin tazobactum (80%) and clindamycin. Both *S. aureus* and MRSA had 100% sensitivity to rifampicin. *S. aureus* has a remarkable ability to develop resistance to any antibiotic [36]. Due to the presence of MRSA in community acquired infections, beta lactum antibiotics are not very effective for treatment and Vancomycin is the agent of choice in serious MRSA infections [36].

The incidence of in hospital mortality (25%) of sepsis was highest among patients with MODS (60%) and septic shock (41.6%). A study done in Northern India had 63.6% mortality in sepsis [20]. A German study had 24.3% in hospital mortality of which septic shock accounted for 58.8% of deaths [37]. In spite of advances in treatment the incidence of mortality in sepsis remains very high probably due to increasing age of patients, emergence of multidrug resistant organisms and use of immunosuppressive medications [37].

LIMITATION

This study had several limitations. Since this was a retrospective study, selection bias could not be eliminated. The data were collected from case records for which accuracy cannot be completely validated. Impact of appropriate antibiotics on outcome could not be assessed. Hence, prospective multicentre studies with large sample size are essential to find out common bacterial pathogens causing sepsis and their antimicrobial sensitivity pattern in this geographical area. This will help in formulating regionally useful empirical treatment guidelines for sepsis.

CONCLUSION

Gram negative organisms were the principal cause of septicaemia in the present study. *Acinetobacter* was resistant to most antibiotics. Cephalosporin resistance was more than 70%. Imipenem, meropenem, amikacin were the most sensitive drugs for Gram negative bacteria. Piperacillin, vancomycin and amikacin are the antimicrobials with higher sensitivity for Gram positive organisms. Therefore, knowledge of bacteriological profile of organisms causing sepsis and antibiotics susceptibility patterns is essential in improving outcome of patients in ICU. Choosing appropriate antibiotics reduces financial burden and also prevents emergence of drug resistant strains.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Feb 02, 2018**
Date of Peer Review: **Mar 06, 2018**
Date of Acceptance: **Mar 29, 2018**
Date of Publishing: **May 01, 2018**